Available online at www.sciencedirect.com

SCIENCE DIRECT®

Vision Research 46 (2006) 467–474

Vision Research

www.elsevier.com/locate/visres

Dopaminergic modulation of horizontal-cell-axon-terminal receptive field size in the mammalian retina ☆

Herbert A. Reitsamer [a,b], Renate Pflug [a,*], Melchior Franz [a], Sonja Huber [a]

[a] *Department of Physiology, Center for Physiology and Pathophysiology, Medical University of Vienna, Austria*
[b] *Department of Opthalmology and Optometry, Paracelsus University, Salzburg, Austria*

Received 3 February 2005; received in revised form 27 April 2005

Abstract

Receptive fields of gap junction-coupled axon terminals of B-type horizontal cells of isolated rabbit retinae were measured by recording light responses to slit shaped light stimuli at different eccentricities from the recording site. The D1/D5 agonist SKF-38393 and the membrane permeant second messenger 8-bromo-cAMP caused decreases of space constants by 20% while the D1/D5 antagonist SCH-23390 increased space constants by 25%. The results of this study indicate that axon terminal receptive fields of the rabbit retina can be modulated by D1/D5 receptor activation based on a cAMP-mediated mechanism. The data also suggest the presence of endogenous dopamine as an agent for axon terminal receptive field size modulation.

Keywords: Retina; Receptive field; Dopamine

1. Introduction

Axon terminals of B-type horizontal cells in the retina of cat and rabbit are homonymously connected by gap junctions (Vaney, 1993) and form a syncytium in the outer plexiform layer separate from the electrically coupled syncytia of A-type and of B-type horizontal cell bodies. While axon terminals receive input from rods only, both types of horizontal cell bodies are part of the cone driven, photopic retinal circuitry. Direct input from cone photoreceptors is mediated by chemical synapses (Boycott, Peichl, & Wassle, 1978), while additional rod input is supplied over gap junctions between rods and cones (Nelson, 1977). Signals of horizontal cell somata are thought to feed back onto cones and in turn influence the gain of the cone synapse (Kamermans & Spekreijse, 1999). Ambient illumination modulates space constants and spread of the tracer Neurobiotin through the networks of A-type and B-type horizontal cells (Xin & Bloomfield, 1999). In A-type horizontal cells of the rabbit retina coupling can be altered by the neuromodulator dopamine in a pH-dependent manner (Hampson, Weiler, & Vaney, 1994); pH-independent dopaminergic modulation of gap junction conductivity and horizontal cell receptive fields by dopamine has been demonstrated in cold blooded vertebrates (Piccolino, Neyton, & Gerschenfeld, 1984) and in mice (He, Weiler, & Vaney, 2000).

Although in a number of species including cat and rabbit, dopamine is mainly released in the proximal retina, dopamine receptors have been found in numerous locations including the distal retina. Dopamine receptors are coupled to G-proteins and are divided into two groups, D1/D5 and D2/D3/D4 receptors. D1/D5 receptors are located on horizontal cells and bipolar

☆ Grant support: Austrian FWF P09670-MED and P12036-MED, Österr. Nationalbank-Jubiläumsfonds 6478, and an institutional Grant by the University of Vienna.
* Corresponding author. Tel.: +43 1 4277 62350; fax +43 1 4277 9623.
E-mail address: renate.pflug@meduniwien.ac.at (R. Pflug).

0042-6989/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.visres.2005.05.010

cells (Behrens & Wagner, 1995; Nguyen-Legros, Simon, Caille, & Bloch, 1997; Nguyen-Legros, Versaux-Botteri, & Vernier, 1999; Veruki & Wassle, 1996). Recently, D1b receptors have also been identified on retinal pigment epithelial cells (Versaux-Botteri, Gibert, Nguyen-Legros, & Vernier, 1997). Single cell RT-PCR revealed D1 receptors in A-type horizontal cells of the rabbit retina (Li, Gaughwin, Li, & He, 2004). D2/D3/D4 receptors were found on photoreceptors and in the inner retina (Nguyen-Legros et al., 1999; Wagner, Luo, Ariano, Sibley, & Stell, 1993). To the best of our knowledge, there are no drugs currently available to distinguish between the D1 and D5 receptor subtypes. In the current manuscript, D1 and D5 receptor subtypes will therefore be referred to as D1/D5 receptors.

Since retinal dopamine release is triggered by light (Boelen, Boelen, & Marshak, 1998; Gustincich, Feigenspan, Wu, Koopman, & Raviola, 1997), it is very likely that dopamine is involved in the light dependent modulation of horizontal cell coupling. The large syncytia of horizontal cell somata in the outer plexiform layer therefore seem to play an important role in the retinal adaptation process of photopic vision.

Rod photoreceptors of cats and rabbits provide signals not only to rod bipolar cells as part of the vertical pathway through the retina, but also to the terminal arborization of the long thin axon that arises from B-type horizontal cells (Nelson, von Litzow, Kolb, & Gouras, 1975). The electroconductive properties of this axon prevent propagation of light evoked signals from the soma to the axon terminal and vice versa. This isolation from the cell body results in purely rod driven light responses of the axon terminal. The output of the rod driven axon terminals is unknown and axon terminals are not integrated in any known transretinal scotopic pathway. Sparse synapses of axon terminals to rod bipolar cells are reported (Linberg & Fisher, 1988). Since the fine branches of axon terminals are hard to penetrate only few electrophysiological recordings exist.

In the present study we show measurements of receptive field sizes of horizontal cell axon terminals with and without the influence of dopaminergic agents. The results exhibit a spatially large syncytium partially uncoupled by dopamine through D1/D5 receptor activation. This is very similar to findings for the parent horizontal cell bodies and suggests that axon terminals may play related roles in retinal circuitry.

2. Methods

All animal procedures were approved by the Institutional Animal Care and Use Committee and conducted in accordance with the ARVO statement for the Use of Animals in Ophthalmic and Vision Research.

2.1. Preparation of the retina

Pigmented Hasenkaninchen rabbits (Belgian Hares, Charles River, 2–2.5 kg) of both sexes were housed for two weeks in the vivarium with food and water ad libitum prior to the experiments. The animals were anesthetized with urethane (1.7 g/kg, i.v.) and the eyes were enucleated under dim red light, after which the animals were euthanized with an overdose of anesthetic. Round retina patches (7 mm) were punched out with a trepan and the neural retina was isolated from the pigment epithelium, choroid, and sclera. The isolated retina was mounted between two nylon grids, placed in a chamber, and superfused with tissue culture medium. Retina and medium were maintained at pH 7.3–7.4 and 32.5–33.5 °C.

2.2. Recording setup

Sharp microelectrodes were pulled from glass capillaries on a microelectrode puller (Model P-87, Sutter Instrument Company, Novato, CA, USA) and filled with 4% Neurobiotin and 1% Lucifer yellow in 0.1 M Tris buffer (pH 7.6). The retinal layers were visualized by a CCD camera under infrared illumination to keep the retina in the dark. Sharp electrodes were guided to the axon terminal layer under visual control with a computer controlled micromanipulator (Reitsamer, Groiss, Franz, & Pflug, 2000).

2.3. Recording protocols

After successful impalement of a horizontal cell, receptive field and intensity response protocols were performed according to a precise timing protocol. Since the interval between the measurements of single receptive fields was chosen 15 min, the retina was prevented from complete dark adaptation. The conditions will therefore be referred to as mesopic throughout this paper. In general, recordings were made from cells of the mid periphery and the periphery of the dorsal and ventral retina. Full field and slit-shaped light stimuli were generated on an optical bench with a 100 W Xenon source and projected onto the retina through the condenser of an inverted microscope (Nikon Diaphot, Optoteam Präzisionsinstrumente GmbH, Vienna, Austria). For measurements of receptive fields, a 140 μm broad and 10 mm long slit shaped stimulus was moved in 70 μm steps along its minor axis from the center toward the periphery. Then the slit was moved back to the center and the measurement continued with stepwise moves toward the periphery on the other side of the receptive field. Receptive fields were measured before and during application of the D1/D5 receptor agonist SKF-38393, the D1/D5 receptor antagonist SCH-23390 and the second messenger 8-Br-cAMP which were added to the

superfusate. The drug pump was started after initial control measurements; then, after an additional 15 min equilibration time, the measurement protocol was repeated. After recordings, Neurobiotin was injected and the retina was processed for morphological identification. Neurobiotin was visualized by using the Elite ABC-Kit (vector), incubation with diaminobenzidine (0.03%) and reaction with H_2O_2 (0.01%).

2.4. Calculation of space constants

The receptive field size of a continuous two dimensional horizontal cell network depends primarily on the relationship of two variables, R_M (the membrane resistance in $\Omega\,cm^{-2}$) and R_S (the sheet resistance between cells due to gap junctional coupling in ohms). Naka and Rushton (1967) defined the space constant $\lambda^2 = R_M \cdot R_S^{-1}$ based on the stimulation of a horizontal cell field with a small light spot at various distances from the recording site. Nelson (1977) adapted the model for slit shaped light stimuli displaced along a single axis.

$$V(x) = E \cdot \sinh\frac{a}{2\lambda} \cdot e^{-\left|\frac{x}{\lambda}\right|}, \quad |x| \geqslant \frac{a}{2}, \tag{1}$$

$$V(x) = E \cdot \left(1 - e^{\frac{-a}{2\lambda}} \cdot \cosh\frac{x}{\lambda}\right), \quad |x| \leqslant \frac{a}{2}, \tag{2}$$

where $V(x)$, cell response; x, distance from center; a, slit width; E, cell response at center stimulation.

Lamb showed that an increase in stimulus intensity causes an increase in space constants; and, at high intensities, light scattering might interfere with the model's basic assumptions. Therefore, the stimulus intensities chosen for receptive field measurements were 2 log units below the maximum response. Amplitudes of receptive field recordings (Fig. 1C) were measured and space constants were calculated according to Eqs. (1) and (2). Fig. 3 shows that the responses are fit well by the equation. The center point was interpolated for steady transition between the left and right curve fits.

2.5. Data analysis

All recordings were carried out with an institutionally developed LabView (National Instruments Austria, Salzburg, Austria) based data acquisition system. Graphic analysis was performed with Sigma Plot (SPSS Inc., Chicago, IL, USA) and a paired t test was used to assess drug effects within groups (SPSS, SPSS Inc., Chicago, IL, USA). P-values less than 0.05 were considered significant. All results are expressed as the means ± standard error.

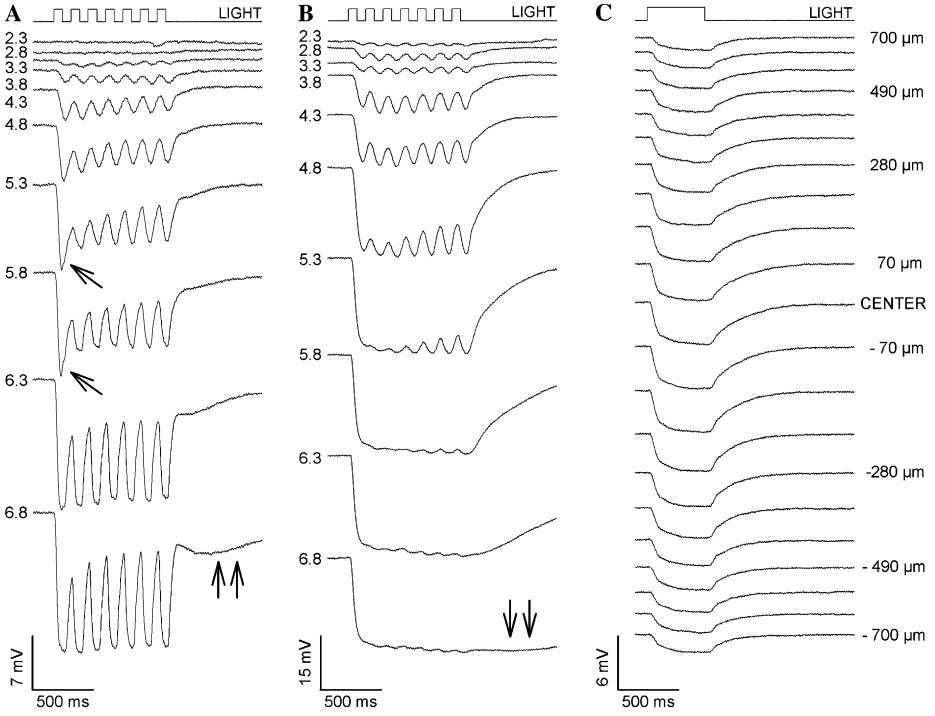

Fig. 1. Intracellular recordings of B-type horizontal cells. (A) Soma and (B) axon terminal responses to flicker stimuli of increasing intensities. Stimulus intensity in log quanta $\mu m^{-2}\,s^{-1}$ is shown on the left side of each tracing, light of 613 nm wavelength was used. Recordings from cell somata show initial overshoots (single arrows) and flicker responses at every light intensity, two criteria that recordings from axon terminals lack consistently in our preparation. In addition somata repolarize quickly after termination of the light stimulus (double upward arrows) while axon terminals repolarize very slowly and stay hyperpolarized for much longer than the somata (double downward arrows). (C) Axon terminal responses to slit shaped single flash stimuli of different eccentricities from the center. Slit eccentricities are shown on the right side of the traces (slit width was 70 µm).

3. Results

3.1. Physiological and morphological identification of axon terminals

Among recordings from rabbit horizontal cells two characteristically different types of responses to full field flickering light stimuli (7 Hz) could be distinguished (see Fig. 1A and Fig. 1B). At low light intensities both response types are similar. Characteristic differences appear in responses to bright light: the responses in Fig. 1B to light intensities $\geqslant 5.8$ log quanta $\mu m^{-2} s^{-1}$ do not follow flicker, they appear saturated and repolarization is very slow suggesting pure rod responses of an axon terminal (Bloomfield & Miller, 1982a). Responses to bright light in Fig. 1A follow flicker promptly. Staining with Neurobiotin after recording of the cell revealed that the response type presented in Fig. 1A belonged to the cell soma, whereas responses of Fig. 1B belonged to axon terminals. We used the failure to follow flickering stimulation with intensities $\geqslant 5.8$ log quanta $\mu m^{-2} s^{-1}$ to identify 25 axon terminal recordings.

Neurobiotin can pass through gap junctions between coupled axon terminals and thus trace a whole network of terminals. The tracer also moves from the axon terminal toward the soma of the horizontal cell. Fig. 2 shows an example of an axon terminal field that has been stained with a single injection of Neurobiotin after recording. The recording site (i.e., injection site) was an axon terminal at the center of the field; it is marked with white arrows. The highlighted cells are drawings that were made under 1000× magnification and transferred into the image. Regardless of their eccentricity, the axons are of similar length (370 ± 15 μm, $n = 6$). To provide better resolution of the details, only half of the field traced by Neurobiotin is shown. All visible somata are stained by dye spread from the axon terminal to the corresponding soma. However, the somata are also coupled by gap junctions and secondary staining from soma to soma can be observed. To provide more detailed information about the shape of an axon terminal, Lucifer yellow was injected into a B-type horizontal cell soma. Neither the B-type horizontal cell somata nor their axon terminals show dye coupling with Lucifer yellow (Vaney, 1993), thus only a single soma with its axon terminal is stained (see drawing in Fig. 2 inset). Since the increasing size of horizontal cell dendritic trees with eccentricity has been characterized thoroughly by Mills and Massey (1994) the size of the stained somata was used to estimate the eccentricity of the recordings (see Section 4).

3.2. Receptive fields of axon terminals and their modulation

Space constants of each axon terminal were determined before and during drug application: responses of axon terminals to single flash stimulation with a slit shaped light stimulus were measured presenting the light stimulus at increasing distances from the site of impalement (Fig. 1C). The decrement of the response amplitudes was used to calculate space constants as an index for the size of the receptive field. Effects of a D1/D5 agonist and a D1/D5 antagonist were investigated. The role of intracellular cAMP concentration was determined by using the membrane permeant cAMP-analogue 8-Br-cAMP.

Fig. 3 shows representative receptive fields of three axon terminals before and during applications of the D1/D5 antagonist SCH-23390 (80 μM), the D1/D5 agonist SKF-38393 (100 μM) and the membrane permeable second messenger 8-Br-cAMP (170 μM). The figure shows that SCH-23390 increases the receptive field size and that SKF-38393 (a D1/D5-agonist) as well as 8-Br-cAMP decrease the sizes of the receptive fields. All receptive field size measurements presented in this study are summarized individually in Fig. 4. Table 1 contains the mean values at baseline and during drug application.

4. Discussion

The present study demonstrates that (a) axon terminals of B-type horizontal cells of the rabbit retina are extensively coupled and form syncytia that collect signals from an area that is about 10 times larger than their dendritic arborization, (b) signal spread in the syncytium of axon terminals of the rabbit retina is attenuated by the neuromodulator dopamine via D1/D5-type receptor activation, and (c) D1/D5 antagonists increase the receptive field size of retinal axon terminals under mesopic conditions indicating the presence of endogenous dopamine.

The use of full field flicker stimuli allowed for discrimination between axon terminal and soma recordings. In addition to the small overshoot at signal onset and a fast repolarisation at signal offset, both of which have been reported previously by others (Bloomfield & Miller, 1982b), we found flicker responses in all somata at all stimulus intensities. In contrast to these findings, all terminals lacked flicker responses at stimulus intensities higher than 5.3–5.8 log quanta $\mu m^{-2} s^{-1}$ (see Fig. 1A and B), consistent with a completely rod driven response. Correct classification by physiological responses was verified by tracer injections after the recordings (e.g., Fig. 2). All cells and terminals of this dataset were stained after recordings and showed the same typical differences in response kinetics.

4.1. Size of space constants

The current study contains a dataset of 25 axon terminals with average space constants of 458 ± 25 μm

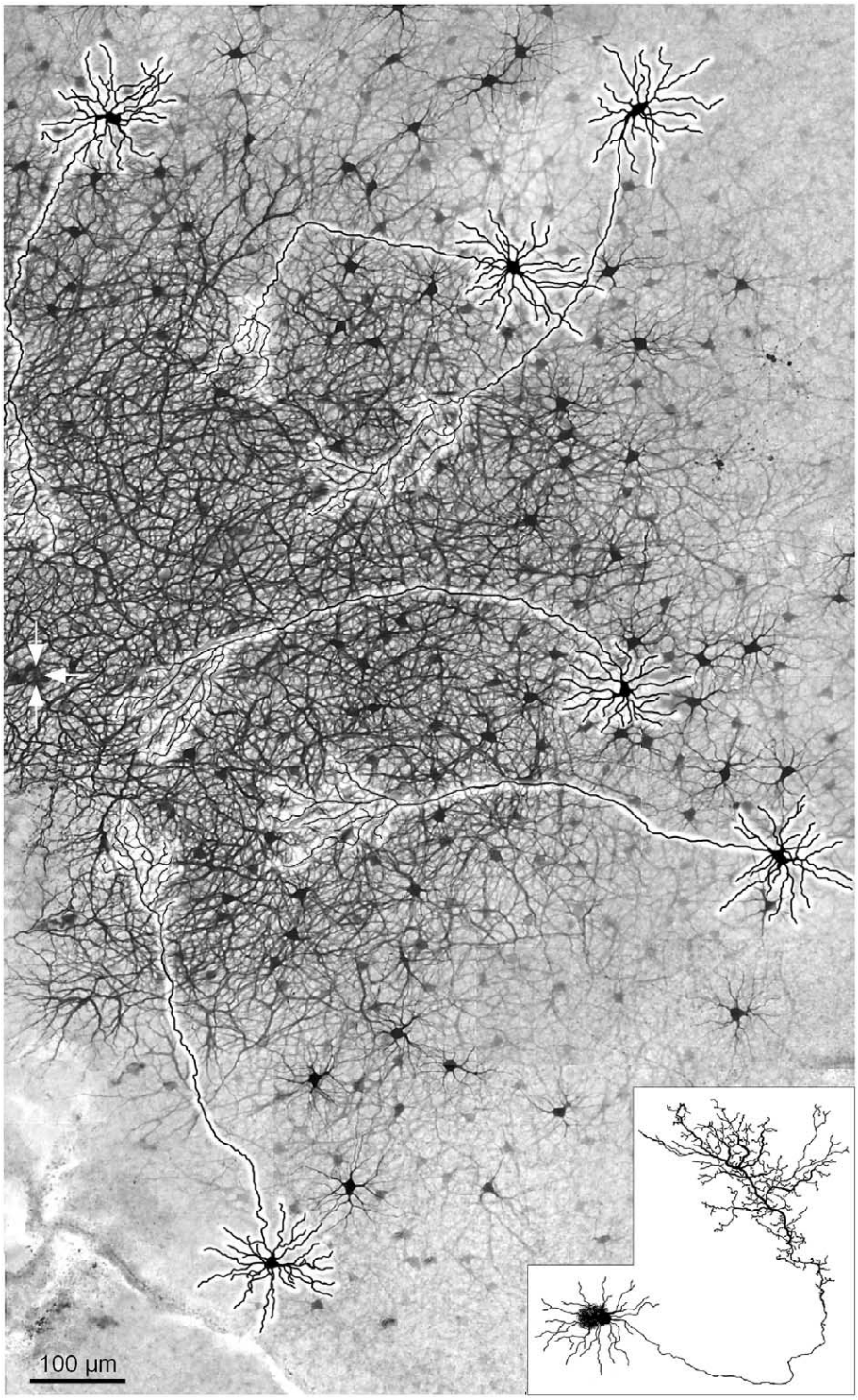

Fig. 2. Image of a flat mounted isolated retina with Neurobiotin tracings of B-type horizontal cells with axon terminals in the inferior mid periphery. After electrophysiological recording the primary axon terminal was injected with Neurobiotin by passing negative current through the recording electrode which spread into all of the coupled terminals shown in this figure (recording/injection site marked with white arrows) and back-stained their cell bodies. Several cells are manually highlighted to show the course of their axon and the position of corresponding terminal within the field and in relation to the cell soma. Mean axon length is 370 ± 15 µm (n = 6). The inset shows a drawing of a single cell after an injection into the soma (see staining artifact) with a more detailed view of the terminal morphology.

under mesopic conditions. The pooled data (n = 52) of all axon terminals recorded during the last four years revealed a mean space constant of 454 ± 35 µm. The mean value of all space constants presented in this study is considerably larger than the space constants measured by Bloomfield, Xin, and Persky, 1995 (69, 104, and

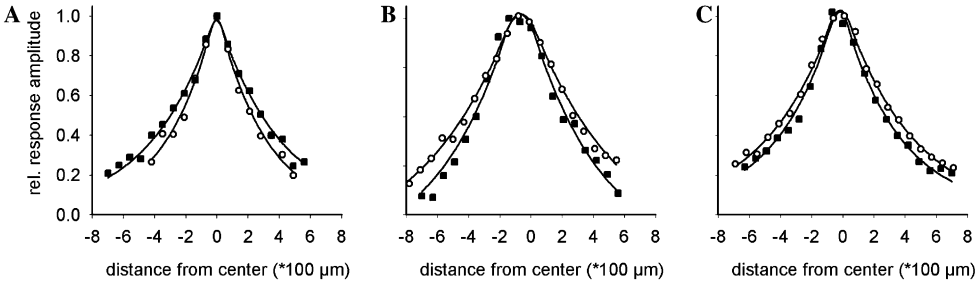

Fig. 3. Effect of drug application on receptive fields of horizontal cell axon terminals. Each of the three panels shows the one dimensional measurement of the receptive field of a single axon terminal before (open symbols) and during (filled symbols) drug application (slit width 140 µm, mesopic conditions). (A) SCH-23390 80 µM (311 µm → 427 µm); (B) SKF-38393 100 µM (588 µm → 464 µm); (C) 8-Br-cAMP 170 µM (443 µm → 360 µm). The data points were fit according to formula (1) and (2) in the methods section.

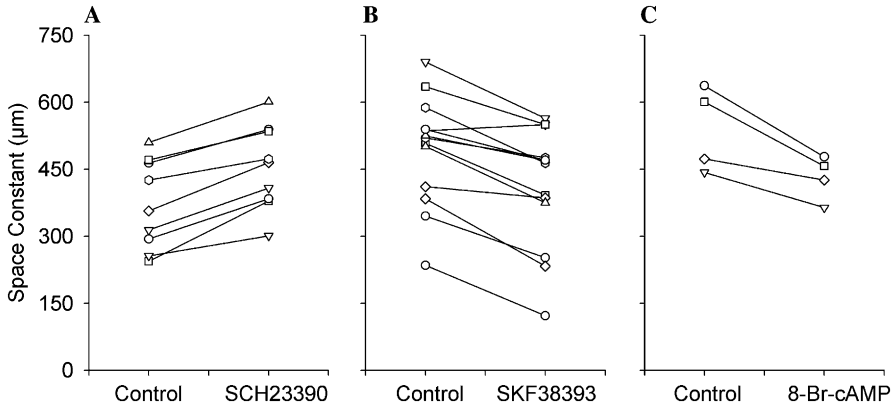

Fig. 4. Space constants of axon terminals before and during drug application under mesopic conditions. Space constants of single axon terminals before and during drug application are connected with lines. (A) D1/D5-antagonist SCH-23390 ($n = 9$, $p < 0.01$); (B) D1/D5-agonist SKF-38393 ($n = 13$, $p < 0.01$); (C) Second messenger 8-bromo-cAMP ($n = 4$, $p = 0.02$).

Table 1
Modulation of space constants of axon terminal receptive fields by a D1/D5-receptor agonist (SKF-38393), a D1/D5-receptor antagonist (SCH-23390), and 8-Br-cAMP

	SCH-23390 ($n = 9$)	SKF-38393 ($n = 13$)	8-Br-cAMP ($n = 4$)
Control	415 ± 32	479 ± 31	539 ± 48
Drug	509 ± 29	393 ± 35	431 ± 49
%-change	+24.9 ± 5	−19.9 ± 4	−19.2 ± 4
P value	<0.01	<0.01	0.02

118 µm), who also used the slit displacement technique as it was used for our experiments. The differences in findings might be explained by the differences in eccentricity of the terminals. The eccentricity of the cells recorded in our study can be estimated from Fig. 2 which shows a representative tracing of an axon terminal field with backfilled B-type horizontal cell somata in the periphery of the rabbit retina. According to Mills and Massey (1994) the diameters of B-type horizontal cell dendritic trees range between 100 and 175 µm in rabbit. The average maximum diameter of the highlighted cells in Fig. 4 is 160 ± 6 µm ($n = 6$) suggesting that the cells were located roughly 9 mm from the center of the retina. This more peripheral location may explain why the space constants of horizontal cell axon terminals presented in the present study are larger than the space constants reported by Bloomfield et al. (1995).

From the extension of the dendritic tree in Fig. 2 and the size of space constants of axon terminals in Table 1 it can be concluded that the collecting area of axon terminals is about 10 times larger than their dendritic area. This confirms previous observations of Vaney (1993) showing that axon terminals of rabbit horizontal cells are homologously coupled by gap junctions similar to horizontal cell somata.

4.2. Modulation of space constants

The light dependent neuromodulator dopamine is known to reduce dye coupling of A-type horizontal cell somata in the rabbit (Hampson et al., 1994), and of the axon bearing horizontal cell somata in the mouse retina (He et al., 2000). Coupling of A-type horizontal cells in rabbit is pH-dependent; dopaminergic modulation is

only possible within a narrow pH range and is maximal at pH 7.2 (Hampson et al., 1994).

Although coupling of axon terminals has been shown previously (Vaney, 1993), evidence for modulation of their receptive field size is lacking. Our studies, carried out at pH 7.4, demonstrate a decrease of space constants of horizontal cell axon terminals by the D1/D5-receptor agonist SKF38393 by 20%. A similar decrease by application of the membrane permeant cAMP-analogue (8-bromo-cAMP) confirmed a cAMP-dependent effect. Reduction of linear space constants by 20% reduces the collecting area of axon terminals by about 35%, a result that is comparable to changes observed for horizontal cell somata in mice (He et al., 2000). The D1/D5 selective antagonist SCH23393 increased space constants by 25% indicating the presence of endogenous dopamine in the semi light adapted retina.

As a consequence the collecting area of axon terminals would almost double during a change from complete dark adaptation to bright light adaptation by increasing from 65% to 125% of its value at mesopic conditions.

4.3. Mechanism of space constant modulation

Dye or tracer spread depends on the conductivity of gap junctions; space constants in this study are calculated from the amplitude of the response to slits flashed at different positions; space constants depend not only on the resistance of gap junctions connecting axon terminals (R_S) but also on their membrane resistance (R_M) according to the formula $\lambda^2 = R_M \cdot R_S^{-1}$ (Lamb, 1976; Naka & Rushton, 1967; Nelson, 1977). Since the space constants presented in this study (458 ± 25 μm, $n = 26$) are clearly larger than the extension of processes in single axon terminal units (about 150 μm, Fig. 2) it seems safe to assume that R_S plays an important role in defining the size of the receptive fields measured. Xin and Bloomfield (1999) have addressed this question in a study comparing light dependent changes of horizontal cell space constants and tracer coupling at various background intensities. Since tracer spread correlates with the coupling resistance, R_S seems to influence space constants more strongly than R_M (Bloomfield & Xin, 1997).

4.4. Connections of axon terminals

The functional significance of receptive field changes depends crucially on how axon terminals are integrated into the retinal circuitry. Axon terminals receive input exclusively from rods. Based on receptive field diameters of about 450 μm as measured in this study and a rod density of 200 000 rods/mm^2 (Famiglietti & Sharpe, 1995) axon terminals might collect and average signals from almost 200 000 rods. The target of their output, though has not been defined yet. Linberg and Fisher (1988) report sparse connections of axon terminals with rod bipolar cells through chemical synapses. This finding is supported by the presence of $GABA_A$ receptors (Vardi & Sterling, 1994) on rod bipolar cell dendrites in macaque and human retinae. Weak staining of $GABA_C$ receptors on dendritic tips of bipolar cell dendrites at their insertion into rod spherules (Enz, Brandstatter, Wassle, & Bormann, 1996) also supports the possibility of a feed forward function of GABAergic axon terminals. Furthermore, immunostaining for GAD67 was shown in invaginating dendrites of axon terminals of B-type horizontal cells (Johnson & Vardi, 1998). Receptive field surround mechanisms as a possible consequence of such a feed forward circuit were not found in rod bipolar cells (Bloomfield & Xin, 2000).

4.5. Axon terminal—photoreceptor feed back

Analogies between horizontal cell soma and axon terminal arrangements in the outer retina suggest a possible involvement of the axon terminal into a feedback loop to rods as it has been outlined for horizontal cell bodies and their feedback to cones. Coupled horizontal cell bodies collect signals from cones. By a negative feedback loop they shift the working range of cones according to mean ambient illumination (Kamermans & Spekreijse, 1999). Attwell, Borges, Wu, and Wilson (1987) found that—although the response range of a rod might reach 25 mV—the synapse to fish horizontal cells rectifies strongly transmitting only potential changes within 5 mV of the rod dark potential. Recent investigations on signal transmission between mammalian rods and rod bipolar cells demonstrate a similar nonlinearity of the synapse of rods to rod bipolar cells, that sets a lower limit to signal transmission at very low light intensities. This threshold has the advantage of eliminating noise at the expense of removing some of the single photon responses (Field & Rieke, 2002). A mathematical model of the rod–rod bipolar cell synapse (van Rossum & Smith, 1998) lead the authors to suggest that a feedback loop of axon terminals might be a suitable neuronal circuit to set such a threshold. The same circuit might be used to keep rod signals inside the working range of bipolar cells at higher light intensities. The large integrating area of axon terminals and its control by the neuromodulator dopamine as demonstrated in this paper highly support such a role of axon terminals.

5. Conclusions

Extensive coupling of axon terminals enables them to collect signals from a large number of rods. The size of the axon terminal receptive field is subject to modulation by the light entrained neuromodulator dopamine. Enlargement of receptive field size by a dopamine

D1/D5 receptor antagonist point to endogenous release of dopamine. Since coupling and neuromodulation patterns are reminescent of horizontal cell somata our findings suggest that axon terminals may play a similar role at the first stage of rod circuitry as horizontal cell somata do for cone circuitry i.e., determine and shift the range of signals transmitted from rods to rod bipolar cells according to mean background illumination.

Acknowledgments

We wish to thank Dr. Astrid Kafka for steady support of this work and Dr. Ralph Nelson for carefully reading and improving the manuscript. We also thank Louise Veres for excellent technical assistance.

References

Attwell, D., Borges, S., Wu, S. M., & Wilson, M. (1987). Signal clipping by the rod output synapse. *Nature, 328*(6130), 522–524.

Behrens, U. D., & Wagner, H. J. (1995). Localization of dopamine D1-receptors in vertebrate retinae. *Neurochemistry International, 27*(6), 497–507.

Bloomfield, S. A., & Miller, R. F. (1982a). A physiological and morphological study of the horizontal cell types of the rabbit retina. *The Journal of Comparative Neurology, 208*(3), 288–303.

Bloomfield, S. A., & Miller, R. F. (1982b). A physiological and morphological study of the horizontal cell types of the rabbit retina. *The Journal of Comparative Neurology, 208*(3), 288–303.

Bloomfield, S. A., & Xin, D. (1997). A comparison of receptive-field and tracer-coupling size of amacrine and ganglion cells in the rabbit retina. *Visual Neuroscience, 14*(6), 1153–1165.

Bloomfield, S. A., & Xin, D. (2000). Surround inhibition of mammalian AII amacrine cells is generated in the proximal retina. *Journal of Physiology, 523*(3), 771–783.

Bloomfield, S. A., Xin, D., & Persky, S. E. (1995). A comparison of receptive field and tracer coupling size of horizontal cells in the rabbit retina. *Visual Neuroscience, 12*(5), 985–999.

Boelen, M. K., Boelen, M. G., & Marshak, D. W. (1998). Light-stimulated release of dopamine from the primate retina is blocked by 1-2-amino-4-phosphonobutyric acid (APB). *Visual Neuroscience, 15*(1), 97–103.

Boycott, B. B., Peichl, L., & Wassle, H. (1978). Morphological types of horizontal cell in the retina of the domestic cat. *Proceedings of The Royal Society of London. Series B. Biological Sciences, 203*(1152), 229–245.

Enz, R., Brandstatter, J. H., Wassle, H., & Bormann, J. (1996). Immunocytochemical localization of the GABAc receptor rho subunits in the mammalian retina. *Journal of Neuroscience, 16*(14), 4479–4490.

Famiglietti, E. V., & Sharpe, S. J. (1995). Regional topography of rod and immunocytochemically characterized "blue" and "green" cone photoreceptors in rabbit retina. *Visual Neuroscience, 12*(6), 1151–1175.

Field, G. D., & Rieke, F. (2002). Nonlinear signal transfer from mouse rods to bipolar cells and implications for visual sensitivity. *Neuron, 34*(5), 773–785.

Gustincich, S., Feigenspan, A., Wu, D. K., Koopman, L. J., & Raviola, E. (1997). Control of dopamine release in the retina: a transgenic approach to neural networks. *Neuron, 18*(5), 723–736.

Hampson, E. C., Weiler, R., & Vaney, D. I. (1994). pH-gated dopaminergic modulation of horizontal cell gap junctions in mammalian retina. *Proceedings of The Royal Society of London. Series B. Biological Sciences, 255*(1342), 67–72.

He, S., Weiler, R., & Vaney, D. I. (2000). Endogenous dopaminergic regulation of horizontal cell coupling in the mammalian retina. *The Journal of Comparative Neurology, 418*(1), 33–40.

Johnson, M. A., & Vardi, N. (1998). Regional differences in GABA and GAD immunoreactivity in rabbit horizontal cells. *Visual Neuroscience, 15*(4), 743–753.

Kamermans, M., & Spekreijse, H. (1999). The feedback pathway from horizontal cells to cones. A mini review with a look ahead. *Vision Research, 39*(15), 2449–2468.

Lamb, T. D. (1976). Spatial properties of horizontal cell responses in the turtle retina. *Journal of Physiology, 263*(2), 239–255.

Li, H., Gaughwin, P., Li, N., & He, S. (2004). Localization of dopamine D1-receptor to A-type horizontal cells in the rabbit retina by single cell RT-PCR. *Neuroscience Letters, 355*(1–2), 146–148.

Linberg, K. A., & Fisher, S. K. (1988). Ultrastructural evidence that horizontal cell axon terminals are presynaptic in the human retina. *The Journal of Comparative Neurology, 268*(2), 281–297.

Mills, S. L., & Massey, S. C. (1994). Distribution and coverage of A- and B-type horizontal cells stained with Neurobiotin in the rabbit retina. *Visual Neuroscience, 11*(3), 549–560.

Naka, K. I., & Rushton, W. A. H. (1967). The generation and spread in fish (cyprinidae). *Journal of Physiology, 192*, 437–461.

Nelson, R. (1977). Cat cones have rod input: a comparison of the response properties of cones and horizontal cell bodies in the retina of the cat. *The Journal of Comparative Neurology, 172*(1), 109–135.

Nelson, R., von Litzow, A., Kolb, H., & Gouras, P. (1975). Horizontal cells in cat retina with independent dendritic systems. *Science, 189*(4197), 137–139.

Nguyen-Legros, J., Simon, A., Caille, I., & Bloch, B. (1997). Immunocytochemical localization of dopamine D1 receptors in the retina of mammals. *Visual Neuroscience, 14*(3), 545–551.

Nguyen-Legros, J., Versaux-Botteri, C., & Vernier, P. (1999). Dopamine receptor localization in the mammalian retina. *Molecular Neurobiology, 19*(3), 181–204.

Piccolino, M., Neyton, J., & Gerschenfeld, H. M. (1984). Decrease of gap junction permeability induced by dopamine and cyclic adenosine 3′:5′-monophosphate in horizontal cells of turtle retina. *Journal of Neuroscience, 4*(10), 2477–2488.

Reitsamer, H., Groiss, H. P., Franz, M., & Pflug, R. (2000). Computer-controlled impalement of cells in retinal wholemounts visualized by infrared CCD imaging on an inverted microscope. *Journal of Neuroscience Methods, 95*(1), 47–53.

van Rossum, M. C., & Smith, R. G. (1998). Noise removal at the rod synapse of mammalian retina. *Visual Neuroscience, 15*(5), 809–821.

Vaney, D. I. (1993). The coupling pattern of axon-bearing horizontal cells in the mammalian retina. *Proceedings of The Royal Society of London. Series B. Biological Sciences, 252*(1334), 93–101.

Vardi, N., & Sterling, P. (1994). Subcellular localization of GABAA receptor on bipolar cells in macaque and human retina. *Vision Research, 34*(10), 1235–1246.

Versaux-Botteri, C., Gibert, J. M., Nguyen-Legros, J., & Vernier, P. (1997). Molecular identification of a dopamine D1b receptor in bovine retinal pigment epithelium. *Neuroscience Letters, 237*(1), 9–12.

Veruki, M. L., & Wassle, H. (1996). Immunohistochemical localization of dopamine D1 receptors in rat retina. *The European Journal Neuroscience, 8*(11), 2286–2297.

Wagner, H. J., Luo, B. G., Ariano, M. A., Sibley, D. R., & Stell, W. K. (1993). Localization of D2 dopamine receptors in vertebrate retinae with anti-peptide antibodies. *The Journal of Comparative Neurology, 331*(4), 469–481.

Xin, D., & Bloomfield, S. A. (1999). Dark- and light-induced changes in coupling between horizontal cells in mammalian retina. *The Journal of Comparative Neurology, 405*(1), 75–87.